

2. NON-TECHNICAL ABSTRACT:

Patients with ovarian cancer that is spread beyond the ovary into the abdominal cavity have a cure rate of less than 20% with the current first-line of chemotherapy. Direct delivery of chemotherapy or biological agents into the peritoneal cavity has produced responses in certain patients whose cancers have persisted after chemotherapy and where the sizes of the individual tumors are small. T-lymphocytes are cells of the immune system that may be activated to produce antitumor effects if these cells receive the proper signals. Tumor cells may "hide" from the immune system by not expressing cell surface molecules that can be recognized by the immune cells. These molecules include a complex protein called the major histocompatibility complex or MHC. MHC proteins are made by cancer cells and by normal cells. The MHC has bound onto it a fragment of a different protein that is produced by the tumor cell. The fragment, which is called a peptide and the MHC proteins to which it is bound, produces the first stimulus to the T-cell. Another protein called B7.1 provides the second important stimulus to the T-cell. A number of animal experiments have shown that the B7.1 protein is necessary for an effective antitumor response by the T-cell. B7.1 is present on certain "professional" antigen presenting cells found normally in the body and called dendritic cells. These cells may have both MHC proteins and costimulatory molecules. Dendritic cells that have both MHC proteins and costimulatory molecules are capable of stimulating T-lymphocytes. Ovarian tumor cells do not normally express the B7.1 protein, and the dendritic cells from the abdomen of patients with ovarian cancer have been found by us to be deficient in the B7.1 protein. A defective avian virus that has not caused harm to patients and normal subjects who have received this virus in other clinical trials, will be introduced into a patient's own cancer cells after being exposed to a small amount of recombinant interferon-gamma. Interferon is used to increase the expression of MHC proteins on the tumor cells. The defective avian virus will in this instance be designed to carry the gene for the human B7.1 protein. The study will determine whether intraperitoneal treatment with irradiated tumor cells after they have been infected with the virus that contains the gene for B7.1, and in combination with intraperitoneal interferon injection, can (a) stimulate the immune system in the abdominal cavity of ovarian cancer patients, (b) whether the treatment is safe, and (c) whether the treatment results in clinical benefit to patients who have previously received standard chemotherapy agents.